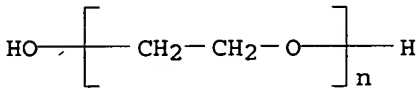
```
=> fil reg; d ide l4; d ide l5
FILE 'REGISTRY' ENTERED AT 10:19:35 ON 08 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    6 MAR 2005  HIGHEST RN 843607-47-6
DICTIONARY FILE UPDATES:   6 MAR 2005  HIGHEST RN 843607-47-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html


L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   25322-68-3  REGISTRY     polyethylene glycol
CN   Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy- (9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   α,ω-Hydroxypoly(ethylene oxide)
CN   α-Hydro-ω-hydroxypoly(oxy-1,2-ethanediyl)
CN   α-Hydro-ω-hydroxypoly(oxyethylene)
CN   1,2-Ethanediol, homopolymer
CN   1660O
CN   1660S
CN   400DAB8
CN   Alkox
CN   Alkox E 100
CN   Alkox E 130
CN   Alkox E 160
CN   Alkox E 240
CN   Alkox E 30
CN   Alkox E 30G
CN   Alkox E 45
CN   Alkox E 60
CN   Alkox E 75
CN   Alkox R 100
CN   Alkox R 1000
CN   Alkox R 15
CN   Alkox R 150
CN   Alkox R 400
CN   Alkox SR
CN   Antarox E 4000
CN   Aquacide III
CN   Aquaffin
CN   Badimol
CN   BDH 301
CN   Bradsyn PEG
CN   Breox 2000
CN   Breox 20M
```

CN Breox 4000
CN Breox 550
CN Breox PEG 300
CN CAFO 154
CN Carbowax
CN Carbowax 100
CN Carbowax 1000
CN Carbowax 1350
CN Carbowax 14000
CN Carbowax 1450
CN Carbowax 1500
CN Carbowax 1540
CN Carbowax 20
CN Carbowax 200
CN Carbowax 20000
CN Carbowax 25000
CN Carbowax 300
CN Carbowax 3350
CN Carbowax 400
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
AR 9002-90-8
DR 615575-04-7, 12676-74-3, 12770-93-3, 9081-95-2, 9085-02-3, 9085-03-4, 174460-08-3, 174460-09-4, 54510-95-1, 125223-68-9, 54847-64-2, 59763-40-5, 64441-68-5, 64640-28-4, 133573-31-6, 25104-58-9, 25609-81-8, 134919-43-0, 101677-86-5, 99264-61-6, 106186-24-7, 112895-21-3, 114323-93-2, 50809-04-6, 50809-59-1, 119219-06-6, 60894-12-4, 61840-14-0, 37361-15-2, 112384-37-9, 67411-64-7, 70926-57-7, 75285-02-8, 75285-03-9, 77986-38-0, 150872-82-5, 154394-38-4, 79964-26-4, 80341-53-3, 85399-22-0, 85945-29-5, 90597-70-9, 88077-80-9, 88747-22-2, 34802-42-1, 107502-63-6, 107529-96-4, 116549-90-7, 156948-19-5, 169046-53-1, 188364-77-4, 188924-03-0, 189154-62-9, 191743-71-2, 196696-84-1, 201163-43-1, 206357-86-0, 221638-71-7, 225502-44-3, 270910-26-4, 307928-07-0, 356055-70-4, 391229-98-4
MF (C2 H4 O)n H2 O
CI PMS, COM
PCT Polyether
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC

(Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

81122 REFERENCES IN FILE CA (1907 TO DATE)
22001 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
81278 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 313377-05-8 REGISTRY
CN Malignostatin (9CI) (CA INDEX NAME)
OTHER NAMES:
CN NK 4
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
32 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
32 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=>

=> fil capl
FILE 'CAPLUS' ENTERED AT 11:15:37 ON 08 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 8 Mar 2005 VOL 142 ISS 11
FILE LAST UPDATED: 7 Mar 2005 (20050307/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que l11; d que l14; d que l30; d que l35

```
L4             1 SEA FILE=REGISTRY ABB=ON  25322-68-3
L5             1 SEA FILE=REGISTRY ABB=ON  313377-05-8
L6            32 SEA FILE=CAPLUS ABB=ON  L5
L7           153 SEA FILE=CAPLUS ABB=ON  (NK4 OR NK 4 OR MALIGNOSTATIN#)/BI
L8          1601 SEA FILE=CAPLUS ABB=ON  PEGYLAT?/BI
L9         79904 SEA FILE=CAPLUS ABB=ON  PEG/OBI OR (POLYETHYLENE/OBI OR POLY
                 ETHYLENE/OBI)(L)GLYCOL#/OBI
L10        81245 SEA FILE=CAPLUS ABB=ON  L4
L11            2 SEA FILE=CAPLUS ABB=ON  (L6 OR L7) AND (L8 OR L9 OR L10)


L5             1 SEA FILE=REGISTRY ABB=ON  313377-05-8
L6            32 SEA FILE=CAPLUS ABB=ON  L5
L7           153 SEA FILE=CAPLUS ABB=ON  (NK4 OR NK 4 OR MALIGNOSTATIN#)/BI
L13        72517 SEA FILE=CAPLUS ABB=ON  POLYOXYALKYLENES/CT
L14            2 SEA FILE=CAPLUS ABB=ON  (L6 OR L7) AND L13


L4             1 SEA FILE=REGISTRY ABB=ON  25322-68-3
L8          1601 SEA FILE=CAPLUS ABB=ON  PEGYLAT?/BI
L9         79904 SEA FILE=CAPLUS ABB=ON  PEG/OBI OR (POLYETHYLENE/OBI OR POLY
                 ETHYLENE/OBI)(L)GLYCOL#/OBI
L10        81245 SEA FILE=CAPLUS ABB=ON  L4
L26         4645 SEA FILE=CAPLUS ABB=ON  HEPATOCYTE GROWTH FACTOR/OBI
L27         1472 SEA FILE=CAPLUS ABB=ON  KRINGLE#/BI
L28         1819 SEA FILE=CAPLUS ABB=ON  HGF##/OBI
L29          114 SEA FILE=CAPLUS ABB=ON  (L26 OR L28) AND L27
L30            2 SEA FILE=CAPLUS ABB=ON  L29 AND (L8 OR L9 OR L10)


L4             1 SEA FILE=REGISTRY ABB=ON  25322-68-3
L8          1601 SEA FILE=CAPLUS ABB=ON  PEGYLAT?/BI
L9         79904 SEA FILE=CAPLUS ABB=ON  PEG/OBI OR (POLYETHYLENE/OBI OR POLY
                 ETHYLENE/OBI)(L)GLYCOL#/OBI
L10        81245 SEA FILE=CAPLUS ABB=ON  L4
L26         4645 SEA FILE=CAPLUS ABB=ON  HEPATOCYTE GROWTH FACTOR/OBI
L28         1819 SEA FILE=CAPLUS ABB=ON  HGF##/OBI
L32         2718 SEA FILE=CAPLUS ABB=ON  CONJUGAT?/OBI(L)(L8 OR L9 OR L10)
L33            9 SEA FILE=CAPLUS ABB=ON  L32 AND (L26 OR L28)
L35            8 SEA FILE=CAPLUS ABB=ON  L33 NOT SURAMIN/OBI
```

=> s l11 or l14 or l30 or l35

```
L80            8 L11 OR L14 OR L30 OR L35
```

```
=> fil uspatf; d que l22; d que l48

FILE 'USPATFULL' ENTERED AT 11:15:39 ON 08 MAR 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 8 Mar 2005 (20050308/PD)
FILE LAST UPDATED: 8 Mar 2005 (20050308/ED)
HIGHEST GRANTED PATENT NUMBER: US6865747
HIGHEST APPLICATION PUBLICATION NUMBER: US2005050605
CA INDEXING IS CURRENT THROUGH 8 Mar 2005 (20050308/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 8 Mar 2005 (20050308/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2004

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from     <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.


L4             1 SEA FILE=REGISTRY ABB=ON  25322-68-3
L5             1 SEA FILE=REGISTRY ABB=ON  313377-05-8
L15            1 SEA FILE=USPATFULL ABB=ON  L5
L17        17460 SEA FILE=USPATFULL ABB=ON  L4
L18         4258 SEA FILE=USPATFULL ABB=ON  PEGYLAT? OR PEGYLAT?/IT
L19       181505 SEA FILE=USPATFULL ABB=ON  (PEG OR (POLYETHYLENE OR POLY
                 ETHYLENE)(L)GLYCOL#)/IT OR PEG OR (POLYETHYLENE OR POLY
                 ETHYLENE)(3A)GLYCOL#
L20        18839 SEA FILE=USPATFULL ABB=ON  POLYOXYALKYLENES/CT
L22            1 SEA FILE=USPATFULL ABB=ON  L15 AND (L17 OR L18 OR L19 OR L20)



L4             1 SEA FILE=REGISTRY ABB=ON  25322-68-3
L17        17460 SEA FILE=USPATFULL ABB=ON  L4
L23       135296 SEA FILE=USPATFULL ABB=ON  CONJUGAT?
L24        13620 SEA FILE=USPATFULL ABB=ON  CONJUGAT?/IT
L37          445 SEA FILE=USPATFULL ABB=ON  (HEPATOCYTE GROWTH FACTOR OR
                 HGF)/IT
L40         4248 SEA FILE=USPATFULL ABB=ON  PEGYLAT?
L42        14632 SEA FILE=USPATFULL ABB=ON  (PEG OR (POLYETHYLENE OR POLY
                 ETHYLENE)(L)GLYCOL#)/IT
L43       178740 SEA FILE=USPATFULL ABB=ON  (PEG OR (POLYETHYLENE OR POLY
```

```
                ETHYLENE)(3A)GLYCOL#)
L44          3058 SEA FILE=USPATFULL ABB=ON  L23(5A)(L40 OR L43)
L45           973 SEA FILE=USPATFULL ABB=ON  L24(L)(L42 OR L17)
L48            11 SEA FILE=USPATFULL ABB=ON  (L44 OR L45) AND L37


=> s l22 or l48

L81            11 L22 OR L48

=> fil toxcenter; d que l53 ; d que l57

FILE 'TOXCENTER' ENTERED AT 11:15:41 ON 08 MAR 2005
COPYRIGHT (C) 2005 ACS


FILE COVERS 1907 TO 1 Mar 2005 (20050301/ED)

This file contains CAS Registry Numbers for easy and accurate substance
identification.

TOXCENTER has been enhanced with new files segments and search fields.
See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary.  See http://www.nlm.nih.gov/mesh/ and
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html for a
description of changes.


L4              1 SEA FILE=REGISTRY ABB=ON  25322-68-3
L5              1 SEA FILE=REGISTRY ABB=ON  313377-05-8
L49            27 SEA FILE=TOXCENTER ABB=ON  L5
L50            78 SEA FILE=TOXCENTER ABB=ON  NK4 OR NK 4 OR MALIGNOSTATIN#
L51          8719 SEA FILE=TOXCENTER ABB=ON  L4
L52         18077 SEA FILE=TOXCENTER ABB=ON  PEG OR PEGYLAT? OR (POLYETHYLENE OR
                  POLY ETHYLENE)(3A)GLYCOL#
L53             2 SEA FILE=TOXCENTER ABB=ON  (L49 OR L50) AND (L51 OR L52)



L4              1 SEA FILE=REGISTRY ABB=ON  25322-68-3
L51          8719 SEA FILE=TOXCENTER ABB=ON  L4
L52         18077 SEA FILE=TOXCENTER ABB=ON  PEG OR PEGYLAT? OR (POLYETHYLENE OR
                  POLY ETHYLENE)(3A)GLYCOL#
L54          2479 SEA FILE=TOXCENTER ABB=ON  HEPATOCYTE GROWTH FACTOR OR HGF
L56         65829 SEA FILE=TOXCENTER ABB=ON  CONJUGAT?
L57             4 SEA FILE=TOXCENTER ABB=ON  L54 AND (L51 OR L52) AND L56


=> s l53 or l57

L82             4 L53 OR L57

=> fil DRUGU, JICST-EPLUS, PASCAL, BIOTECHNO, ESBIOBASE, BIOSIS, LIFESCI,BIOTECHDS, WPIDS

FILE 'DRUGU' ENTERED AT 11:15:42 ON 08 MAR 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE 'JICST-EPLUS' ENTERED AT 11:15:42 ON 08 MAR 2005
COPYRIGHT (C) 2005 Japan Science and Technology Agency (JST)
```

FILE 'PASCAL' ENTERED AT 11:15:42 ON 08 MAR 2005

FILE 'BIOTECHNO' ENTERED AT 11:15:42 ON 08 MAR 2005

FILE 'ESBIOBASE' ENTERED AT 11:15:42 ON 08 MAR 2005

FILE 'BIOSIS' ENTERED AT 11:15:42 ON 08 MAR 2005

FILE 'LIFESCI' ENTERED AT 11:15:42 ON 08 MAR 2005

FILE 'BIOTECHDS' ENTERED AT 11:15:42 ON 08 MAR 2005

FILE 'WPIDS' ENTERED AT 11:15:42 ON 08 MAR 2005


```
=> d que l62; d que l65

L58          384 SEA NK4 OR NK 4 OR MALIGNOSTATIN#
L60       116483 SEA PEG OR PEGYLAT? OR (POLYETHYLENE OR POLY ETHYLENE)(3A)
                 GLYCOL#
L62            1 SEA L58 AND L60


L59        17637 SEA HGF OR HEPATOCYTE GROWTH FACTOR
L60       116483 SEA PEG OR PEGYLAT? OR (POLYETHYLENE OR POLY ETHYLENE)(3A)
                 GLYCOL#
L61       303931 SEA CONJUGAT?
L63           12 SEA L60 AND L59 AND L61
L65           11 SEA L63 NOT SURAMIN


=> s l62 or l65

L83           11 L62 OR L65

=> fil medl cancer; d que l73

FILE 'MEDLINE' ENTERED AT 11:15:48 ON 08 MAR 2005

FILE 'CANCERLIT' ENTERED AT 11:15:48 ON 08 MAR 2005


L66           91 SEA NK4 OR NK 4 OR MALIGNOSTATIN#
L67         4878 SEA HEPATOCYTE GROWTH FACTOR/CT
L72        18756 SEA POLYETHYLENE GLYCOLS/CT
L73            1 SEA (L66 OR L67) AND L72


=> fil embase; d que l79

FILE 'EMBASE' ENTERED AT 11:15:50 ON 08 MAR 2005
```

FILE COVERS 1974 TO 3 Mar 2005 (20050303/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L74          66 SEA FILE=EMBASE ABB=ON  NK4 OR NK 4 OR MALIGNOSTATIN#
L75        4242 SEA FILE=EMBASE ABB=ON  SCATTER FACTOR
L76        3340 SEA FILE=EMBASE ABB=ON  HEPATOCYTE GROWTH FACTOR
L77       10913 SEA FILE=EMBASE ABB=ON  MACROGOL/CT OR MACROGOL DERIVATIVE/CT
L78          11 SEA FILE=EMBASE ABB=ON  PEGYLATION/CT
L79           2 SEA FILE=EMBASE ABB=ON  (L74 OR L75 OR L76) AND (L77 OR L78)

=> dup rem l73, l80, l79, l82, l83, l81
FILE 'MEDLINE' ENTERED AT 11:16:16 ON 08 MAR 2005

FILE 'CAPLUS' ENTERED AT 11:16:16 ON 08 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 11:16:16 ON 08 MAR 2005
COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.

FILE 'TOXCENTER' ENTERED AT 11:16:16 ON 08 MAR 2005
COPYRIGHT (C) 2005 ACS

FILE 'BIOTECHDS' ENTERED AT 11:16:16 ON 08 MAR 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE 'WPIDS' ENTERED AT 11:16:16 ON 08 MAR 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE 'USPATFULL' ENTERED AT 11:16:16 ON 08 MAR 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L73
PROCESSING COMPLETED FOR L80
PROCESSING COMPLETED FOR L79
PROCESSING COMPLETED FOR L82
PROCESSING COMPLETED FOR L83
PROCESSING COMPLETED FOR L81
L84          26 DUP REM L73 L80 L79 L82 L83 L81 (11 DUPLICATES REMOVED)
                ANSWER '1' FROM FILE MEDLINE
                ANSWERS '2-9' FROM FILE CAPLUS
                ANSWERS '10-11' FROM FILE EMBASE
                ANSWER '12' FROM FILE TOXCENTER
                ANSWERS '13-14' FROM FILE BIOTECHDS
                ANSWERS '15-18' FROM FILE WPIDS
                ANSWERS '19-26' FROM FILE USPATFULL

=> d iall 1; d ibib ed abs hitrn 2-9; d iall 10-18; d ibib abs hitrn 19-26; fil hom

L84  ANSWER 1 OF 26      MEDLINE on STN
ACCESSION NUMBER:    2004284717      MEDLINE
DOCUMENT NUMBER:     PubMed ID: 15184822
TITLE:               Current status of the use of growth factors and other
                     adjuvant medications in patients receiving peginterferon
```

and ribavirin.
AUTHOR: Kontorinis Nickolas; Agarwal Kaushik; Dieterich Douglas T
CORPORATE SOURCE: Department of Medicine, Mount Sinai Hospital, New York, NY, USA.
SOURCE: Reviews in gastroenterological disorders, (2004) 4 Suppl 1 S39-47. Ref: 65
Journal code: 101140143. ISSN: 1533-001X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040609
Last Updated on STN: 20040624
Entered Medline: 20040618

ABSTRACT:
Hepatitis C virus (HCV) is the most common chronic infection in the United States, affecting almost 3.9 million Americans. The most effective treatment for chronic HCV infection is combination antiviral therapy with peginterferon and ribavirin. However, combination therapy is also associated with significant adverse effects and is contraindicated in certain patient populations. Hematological adverse effects are common and are a frequent cause of dose reduction and interruption or discontinuation of therapy. Currently there are no approved treatments for the hematological adverse events associated with HCV therapy. However, emerging data suggest that utilization of hematopoietic growth factors can provide a useful adjunct to treatment and optimize sustained virologic response rates.

CONTROLLED TERM: Check Tags: Comparative Study; Female; Male
Antiviral Agents: AE, adverse effects
*Antiviral Agents: TU, therapeutic use
Chemotherapy, Adjuvant
Drug Therapy, Combination
*Erythropoietin, Recombinant: TU, therapeutic use
*Hepacivirus: DE, drug effects
Hepacivirus: IP, isolation & purification
Hepatitis C, Chronic: DI, diagnosis
*Hepatitis C, Chronic: DT, drug therapy
Hepatitis C, Chronic: MO, mortality
***Hepatocyte Growth Factor: TU, therapeutic use**
Humans
Interferon Alfa-2a: TU, therapeutic use
Polyethylene Glycols: TU, therapeutic use
Ribavirin: AE, adverse effects
Ribavirin: TU, therapeutic use
Risk Assessment
Severity of Illness Index
Treatment Outcome
Viral Load
CAS REGISTRY NO.: 36791-04-5 (Ribavirin); 67256-21-7 (Hepatocyte Growth Factor); 76543-88-9 (Interferon Alfa-2a)
CHEMICAL NAME: 0 (Antiviral Agents); 0 (Erythropoietin, Recombinant); 0 (Polyethylene Glycols); 0 (peginterferon alfa-2a)

L84 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:756735 CAPLUS
DOCUMENT NUMBER: 141:271538
TITLE: Peptide ligands for the c-Met receptor as antagonists

of **hepatocyte growth factor** and their use in cancer therapy

INVENTOR(S): Sato, Aaron K.; Dransfield, Daniel T.; Ladner, Robert C.; Shrivastava, Ajay; Nanjappan, Palaniappa

PATENT ASSIGNEE(S): Dyax Corp., USA; Bracco International B.V.

SOURCE: PCT Int. Appl., 174 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078778	A2	20040916	WO 2004-US6473	20040303
WO 2004078778	A3	20041118		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-451588P P 20030303

OTHER SOURCE(S): MARPAT 141:271538

ED Entered STN: 16 Sep 2004

AB Peptides that can bind to the c-met receptor and antagonize hepatocyte growth factor (HGF) are described for use in the diagnosis and treatment of c-met-dependent cancers. Antagonism of hepatocyte can slow tumor growth and can also increase the sensitivity of affected cells to DNA-damaging cytotoxic agents used in cancer chemotherapy. These peptides may also be used in imaging agents for cancer diagnosis and surveillance. Peptides were selected from phage display libraries using soluble c-Met of c-Met bearing DLD-1 cells to screen. Competition ELISAs were used to demonstrate the ability of these peptides to block HGF binding to c-Met and prevented HGF stimulation of cell proliferation.

IT **25322-68-3D, Polyethylene glycol, conjugates** with **hepatocyte growth factor** antagonists
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum stability of; peptide ligands for c-Met receptor as antagonists of **hepatocyte growth factor** and their use in cancer therapy)

L84 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:203710 CAPLUS

DOCUMENT NUMBER: 140:223336

TITLE: Scatter factor/**hepatocyte growth factor** antagonist **NK4** for the treatment of glioma

INVENTOR(S): Brandt, Michael; Brockmann, Marc; Lamszus, Katrin; Papadimitriou, Apollon; Schuell, Christine

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004019991	A2	20040311	WO 2003-EP9545	20030828
WO 2004019991	A3	20040415		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1393748	A1	20040303	EP 2002-19137	20020830

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

US 2004110685	A1	20040610	US 2003-651807	20030829

PRIORITY APPLN. INFO.: EP 2002-19137 A 20020830

ED Entered STN: 14 Mar 2004

AB A pharmaceutical composition for the treatment of a tumor derived from glia cells of the central nervous system of a patient is characterized in that the composition contains a pharmaceutically effective amount of a fragment of the hepatocyte growth factor, said fragment consisting of the N-terminal hairpin domain and the four **kringle** domains of the hepatocyte growth factor α-chain.

IT **25322-68-3DP, Polyethylene glycol, conjugates** with **NK4 313377-05-8DP, NK4 , conjugates** with **polyethylene glycol**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(scatter factor/**hepatocyte growth factor** fragment **NK4** for the treatment of glioma)

L84 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:269695 CAPLUS
DOCUMENT NUMBER: 140:309369
TITLE: Polyoxyalkylene conjugates with bioactive compounds with decreased antigenicity
INVENTOR(S): Martinez, Alexa L.; Sherman, Merry R.; Saifer, Mark G. P.; Williams, L. David
PATENT ASSIGNEE(S): Mountain View Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 35 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004062748	A1	20040401	US 2002-317092	20021212
US 2004062746	A1	20040401	US 2003-669597	20030925
WO 2004030617	A2	20040415	WO 2003-US29989	20030925

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,

OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-414424P P 20020930
US 2002-317092 A2 20021212

ED Entered STN: 02 Apr 2004

AB Methods are provided for the preparation of conjugates of a variety of bioactive components, especially proteins, with water-soluble polymers (e.g., polyethylene glycol and derivs.), and the conjugates have reduced antigenicity and immunogenicity compared to similar conjugates prepared by using polyethylene glycol containing a methoxyl or another alkoxyl group. The invention also provides conjugates prepared by such methods, compns. comprising such conjugates, kits containing such conjugates or compns. and methods of use of the conjugates and compns. in diagnostic and therapeutic protocols. PEG-monoaldehyde was obtained from PEG by treatment with 3-chloropropionaldehyde di-Et acetal in 3 steps. The use of monofunctionally activated PEG that does not contain a methoxyl group or another alkoxyl group for the synthesis of protein conjugates resulted in conjugates with decreased immunoreactivity. The resultant conjugates had decreased antigenicity, i.e., decreased ability to interact with antibodies developed against mPEG conjugates of the same protein, and decreased immunogenicity, i.e., decreased ability to evoke an immune response against the PEG component.

IT **25322-68-3, Polyethylene glycol**
RL: RCT (Reactant); RACT (Reactant or reagent)
(polyoxyalkylene **conjugates** with bioactive compds. with decreased antigenicity)

L84 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2004:267163 CAPLUS
DOCUMENT NUMBER: 140:309364
TITLE: Polyoxyalkylene conjugates with bioactive compounds with decreased antigenicity
INVENTOR(S): Martinez, Alexa L.; Sherman, Merry R.; Saifer, Mark G. P.; Williams, L. David
PATENT ASSIGNEE(S): Mountain View Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 317,092.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004062746	A1	20040401	US 2003-669597	20030925
US 2004062748	A1	20040401	US 2002-317092	20021212

PRIORITY APPLN. INFO.: US 2002-414424P P 20020930
US 2002-317092 A2 20021212

ED Entered STN: 01 Apr 2004

AB Methods are provided for the preparation of conjugates of a variety of bioactive components, especially proteins, with water-soluble polymers (e.g., polyethylene glycol and derivs.), and the conjugates have reduced antigenicity and immunogenicity compared to similar conjugates prepared using polyethylene glycol containing a methoxyl or another alkoxyl group. The invention also provides conjugates prepared by such methods, compns. comprising such conjugates, kits containing such conjugates or compns. and methods of use of the conjugates and compns. in diagnostic and therapeutic

protocols. PEG-monoaldehyde was obtained from PEG by treatment with 3-chloropropionaldehyde di-Et acetal in 3 steps. The use of monofunctionally activated PEG that does not contain a methoxyl group or another alkoxyl group for the synthesis of protein conjugates resulted in conjugates with decreased immunoreactivity. The resultant conjugates had decreased antigenicity, i.e., decreased ability to interact with antibodies developed against mPEG conjugates of the same protein, and decreased immunogenicity, i.e., decreased ability to evoke an immune response against the PEG component.

IT **25322-68-3, Polyethylene glycol**
RL: RCT (Reactant); RACT (Reactant or reagent)
(polyoxyalkylene **conjugates** with bioactive compds. with decreased antigenicity)

L84 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2003:971712 CAPLUS
DOCUMENT NUMBER: 140:31479
TITLE: Solid phase method for preparation of peptide-lipid conjugates for targeted liposome formulations
INVENTOR(S): Wu, Shih-Kwang; Chang, Ting-Gung; Tseng, Chin-Lu; Chen, Li-Jung; Shih, Kae-Shyang
PATENT ASSIGNEE(S): Development Center for Biotechnology, Taiwan
SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S. Pat. Appl. 2003 229,013.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003229017	A1	20031211	US 2002-308644	20021203
US 2003229013	A1	20031211	US 2001-16569	20011207
CA 2413629	AA	20030607	CA 2002-2413629	20021205
CN 1453293	A	20031105	CN 2002-155769	20021209

PRIORITY APPLN. INFO.: US 2001-16569 A2 20011207
ED Entered STN: 14 Dec 2003
AB A solid phase synthesis method for preparing peptide-spacer-lipid conjugates, the peptide-spacer-lipid conjugates synthesized by the method, and liposomes containing the peptide-spacer-lipid conjugates. The present invention provides a convenient solid phase synthesis method for preparing peptide-spacer-lipid conjugates and provides various linkage groups (such as amide group) for conjugating peptide, spacer and lipid, wherein the spacer may comprise PEG. Several advantages can be achieved, such as the synthetic procedure can be simplified, the synthesis process can be set to automation, the purification is easier in each reaction step, and the product losses can be reduced to minimal during synthesis. The present synthetic method is suitable for preparing a wide range of peptide-spacer-lipid conjugates, provides a peptide-spacer-lipid conjugate prepared by the solid phase synthesis method of the present invention, which can be incorporated into a liposome as the targeting moiety for liposomal drug delivery to specific cells, and provides a targeting liposome containing the present peptide-spacer-lipid conjugate. Thus, DSPE-NHCO-PEG-CONH-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol (prepared by a solid-phase peptide method) and mPEG-DSPE were dissolved in CHCl3/MeOH (1:1) and evaporated to make a lipid film. The dried lipid film was hydrated in HEPES and NaCl. After the lipid film melted and the mixture turned to a clear micellar solution, the micellar solution was then transferred into 4 mL DOX contained liposomes (contained 0.21 mmol total lipids and 0.058 mmol DOX.HCl) at 60° C. for 4 h to complete the insertion. The solution is then passed through a gel filtration column, such as SepharoseTM CL-4B (Pharmacia BiotechTM) column,

to sep. micelles and targeted therapeutic liposomes. Fractions of micelles and targeted therapeutic liposomes were pooled sep. for quant. analyses. The inserted peptide-PEG-lipid conjugates in liposomes were about 1% of the total lipid of liposomes.

IT **25322-68-3, Polyethylene glycol**
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid phase method for preparation of peptide-lipid **conjugates** for targeted liposome formulations)

L84 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2002:656007 CAPLUS
DOCUMENT NUMBER: 137:174894
TITLE: **PEG-conjugates** of **HGF-NK4**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1234583	A1	20020828	EP 2001-104640	20010223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2438308	AA	20020926	CA 2002-2438308	20020221
WO 2002074344	A2	20020926	WO 2002-EP1837	20020221
WO 2002074344	A3	20031204		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003012775	A1	20030116	US 2002-81309	20020221
EP 1389132	A2	20040218	EP 2002-700263	20020221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004521139	T2	20040715	JP 2002-573051	20020221
BR 2002007510	A	20040727	BR 2002-7510	20020221
NO 2003003737	A	20031021	NO 2003-3737	20030822
BG 108125	A	20040930	BG 2003-108125	20030822

PRIORITY APPLN. INFO.:

EP 2001-104640	A	20010223
WO 2002-EP1837	W	20020221

ED Entered STN: 30 Aug 2002

AB A conjugate comprising an N-terminal fragment of hepatocyte growth factor (HGF/SF) consisting of the hairpin domain and the four **kringle** regions of the α-chain and one to three polyethylene glycol group(s), said polyethylene glycol group(s) having an overall mol. weight of from about 10 to 40 kDa, has improved properties and is a useful therapeutic agent for tumor treatment.

IT **25322-68-3D, Polyethylene glycol, HGF-NK4 conjugates**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**PEG-conjugates** of **HGF-NK4** for antitumor use)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:849373 CAPLUS
DOCUMENT NUMBER: 137:358081
TITLE: Diagnostic imaging compositions, their methods of synthesis, and use
INVENTOR(S): Li, Chun; Wen, Xiaoxia; Wu, Qing-Ping; Wallace, Sydney; Ellis, Lee M.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002087498	A2	20021107	WO 2002-US12510	20020419
WO 2002087498	A3	20031030		
WO 2002087498	C1	20031211		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2444483	AA	20021107	CA 2002-2444483	20020419
US 2002197261	A1	20021226	US 2002-126369	20020419
US 2003003048	A1	20030102	US 2002-126216	20020419
EP 1389090	A2	20040218	EP 2002-766783	20020419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:		
US 2001-286453P	P	20010426
US 2001-334969P	P	20011204
US 2001-343147P	P	20011220
WO 2002-US12510	W	20020419

ED Entered STN: 08 Nov 2002
AB Conjugate mols. comprising a ligand bonded to a polymer are disclosed. One such conjugate mol. comprises a ligand bonded to a polymer, a chelating agent bonded to the polymer, and a radioisotope chelated to the chelating agent. The conjugate mols. may be useful in detecting and/or treating tumors or biol. receptors. These conjugate mols. may be synthesized without the necessity of preactivation of the ligand using an SCN-polymer-chelating agent precursor. Conjugate mols. incorporating an annexin V ligand are particularly useful for visualizing apoptotic cells. Conjugate mols. incorporating a C225 ligand are particularly useful for targeting tumors expressing EGFR.
IT **25322-68-3DP**, **PEG**, radiolabeled **conjugates**
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(diagnostic imaging compns. comprising radiolabeled **conjugates**
)

L84 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:747647 CAPLUS

DOCUMENT NUMBER: 135:308875
TITLE: Drugs retained in target tissue over long time
INVENTOR(S): Sato, Haruya; Hayashi, Eiko; Shirae, Hideyuki
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074399	A1	20011011	WO 2001-JP2604	20010328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001044602	A5	20011015	AU 2001-44602	20010328
EP 1279405	A1	20030129	EP 2001-917574	20010328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003103934	A1	20030605	US 2002-259773	20020930
PRIORITY APPLN. INFO.:			JP 2000-93775 A	20000330
			WO 2001-JP2604 W	20010328

ED Entered STN: 12 Oct 2001

AB Disclosed are a ligand attached to a polyethylene glycol wherein a polyethylene glycol chain is attached to a ligand having a binding affinity to a specific receptor or a protein (antigen, etc.) located on the cell membrane of a target tissue and being capable of avoiding the incorporation into cells; and medicines wherein a drug (a physiol. active substance, etc.) is attached to this polyethylene glycol chain. Thus, a novel ligand, which can be accumulated at a high concentration around a target tissue and has good retention properties in the blood, and excellent medicines, wherein a drug (a physiol. active substance, etc.) efficacious in the above target tissue is attached thereto, can be provided. (Gal)3-polyethylene glycol-interferon-α conjugate was prepared and administered to mice; higher concns. of interferons were determined in the plasma and liver tissues, as compared to the ones obtained by administration of unmodified interferons.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 10 OF 26 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004117609 EMBASE
TITLE: Reversal of liver fibrosis and cirrhosis - An emerging reality.
AUTHOR: Fallowfield J.A.; Iredale J.P.
CORPORATE SOURCE: Prof. J.P. Iredale, Liver Research Group, Southampton General Hospital, Tremona Road, Southampton SO16 6YD, United Kingdom. jpi@soton.ac.uk
SOURCE: Scottish Medical Journal, (2004) 49/1 (3-6).
Refs: 30

ISSN: 0036-9330 CODEN: SMDJAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 009 Surgery
022 Human Genetics
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
In summary, there are compelling data demonstrating proof-of-concept that even advanced fibrosis and cirrhosis are reversible states. The molecular mechanisms mediating recovery are becoming increasingly clear, giving real hope of impacting therapeutically on this serious disease.

CONTROLLED TERM: Medical Descriptors:
*liver fibrosis: CO, complication
*liver fibrosis: DI, diagnosis
*liver fibrosis: DT, drug therapy
*liver fibrosis: ET, etiology
*liver cirrhosis: CO, complication
*liver cirrhosis: DI, diagnosis
*liver cirrhosis: DT, drug therapy
*liver cirrhosis: ET, etiology
fibrogenesis
clinical feature
remission
immunosuppressive treatment
chronic hepatitis: DT, drug therapy
decompression surgery
chronic pancreatitis: SU, surgery
treatment outcome
drug mechanism
drug targeting
human
nonhuman
clinical trial
note
Drug Descriptors:
immunosuppressive agent
lamivudine: DT, drug therapy
alpha interferon: DT, drug therapy
interferon: CT, clinical trial
interferon: CB, drug combination
interferon: DT, drug therapy
interferon: PR, pharmaceutics
macrogol
ribavirin: CT, clinical trial
ribavirin: CB, drug combination
ribavirin: DT, drug therapy
corticosteroid: PD, pharmacology
colchicine: PD, pharmacology
tranilast: PD, pharmacology
captopril: PD, pharmacology
malotilate: PD, pharmacology
interleukin 1 receptor blocking agent: PD, pharmacology
recombinant interleukin 10: PD, pharmacology
antioxidant: PD, pharmacology
alpha tocopherol: PD, pharmacology
silymarin: PD, pharmacology

s adenosylmethionine: PD, pharmacology
scatter factor: PD, pharmacology
phosphatidylcholine: PD, pharmacology
peroxisome proliferator activated receptor: PD, pharmacology
herbaceous agent: PD, pharmacology
protein tyrosine kinase inhibitor: PD, pharmacology
fibroblast growth factor: PD, pharmacology
transforming growth factor beta antibody: PD, pharmacology
endothelin receptor antagonist: PD, pharmacology
bosentan: PD, pharmacology
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
gliotoxin: PD, pharmacology
metalloproteinase: PD, pharmacology
unindexed drug

CAS REGISTRY NO.: (lamivudine) 134678-17-4, 134680-32-3; (macrogol) 25322-68-3; (ribavirin) 36791-04-5; (colchicine) 64-86-8; (tranilast) 53902-12-8; (captopril) 62571-86-2; (malotilate) 50512-35-1, 59937-28-9; (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4, 58-95-7, 59-02-9; (silymarin) 65666-07-1; (s adenosylmethionine) 29908-03-0, 485-80-3; (**scatter factor**) 67256-21-7, 72980-71-3; (phosphatidylcholine) 55128-59-1, 8002-43-5; (fibroblast growth factor) 62031-54-3; (bosentan) 147536-97-8, 157212-55-0; (gliotoxin) 37273-88-4, 67-99-2; (metalloproteinase) 81669-70-7

L84 ANSWER 11 OF 26 EMBASE
on STN

ACCESSION NUMBER: 2003349890 EMBASE
TITLE: Tissue regeneration based on growth factor release.
AUTHOR: Tabata Y.
CORPORATE SOURCE: Dr. Y. Tabata, Inst. for Frontier Medical Sciences, Kyoto University, 53 Kawara-cho Shogoin, Sakyo-ku, Kyoto 606-8507, Japan. yasuhiko@frontier.kyoto-u.ac.jp
SOURCE: Tissue Engineering, (2003) 9/SUPPL. 1 (S5-S15).
Refs: 74
ISSN: 1076-3279 CODEN: TIENFP
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:

Tissue engineering is an emerging biomedical field intended to assist the regeneration of body tissue defects too large to self-repair as well as to substitute for the biological functions of damaged and injured organs by using cells with proliferative and differentiative potential. In addition to basic research on such cells, it is undoubtedly indispensable for successful tissue engineering to create an artificial environment enabling cells to induce tissue regeneration. Such an environment can be achieved by making use of a scaffold for cell proliferation and differentiation and for growth factors, as well as their combination. Growth factors are often required to promote tissue regeneration, as they can induce angiogenesis, which supplies oxygen and nutrients to cells transplanted for organ substitution to maintain their biological functions. However, the biological effects of growth factors cannot always be expected because of their poor in vivo stability, unless a drug delivery system is contrived. In this article, tissue regeneration based on the release of growth factors is reviewed to emphasize the significance of drug

delivery systems in tissue engineering.

CONTROLLED TERM: Medical Descriptors:
*tissue regeneration
*tissue engineering
protein secretion
medical technology
medical research
cell proliferation
cell differentiation
drug delivery system
hydrogel
human
nonhuman
review
priority journal
Drug Descriptors:
*growth factor: PR, pharmaceutics
bone morphogenetic protein: PR, pharmaceutics
bone morphogenetic protein 2: PR, pharmaceutics
osteogenic protein 1: PR, pharmaceutics
epidermal growth factor: PR, pharmaceutics
acidic fibroblast growth factor: PR, pharmaceutics
basic fibroblast growth factor: PR, pharmaceutics
nerve growth factor: PR, pharmaceutics
transforming growth factor beta1: PR, pharmaceutics
platelet derived growth factor BB: PR, pharmaceutics
vasculotropin: PR, pharmaceutics
scatter factor: PR, pharmaceutics
somatomedin C: PR, pharmaceutics
polylactic acid: PR, pharmaceutics
collagen: PR, pharmaceutics
calcium phosphate: PR, pharmaceutics
hydroxyapatite: PR, pharmaceutics
microsphere: PR, pharmaceutics
gelatin: PR, pharmaceutics
agarose: PR, pharmaceutics
polyvinyl alcohol: PR, pharmaceutics
macrogol: PR, pharmaceutics
alginic acid: PR, pharmaceutics
heparin: PR, pharmaceutics
amylopectin: PR, pharmaceutics
ethylene vinyl acetate copolymer: PR, pharmaceutics
polyglactin: PR, pharmaceutics
chitosan: PR, pharmaceutics
titanium: PR, pharmaceutics

CAS REGISTRY NO.: (epidermal growth factor) 62229-50-9; (acidic fibroblast growth factor) 106096-92-8; (basic fibroblast growth factor) 106096-93-9; (nerve growth factor) 9061-61-4; (vasculotropin) 127464-60-2; (**scatter factor**) 67256-21-7, 72980-71-3; (somatomedin C) 67763-96-6; (polylactic acid) 26100-51-6; (collagen) 9007-34-5; (calcium phosphate) 10103-46-5, 13767-12-9, 14358-97-5, 7758-87-4; (hydroxyapatite) 1306-06-5, 51198-94-8; (gelatin) 9000-70-8; (agarose) 9012-36-6; (polyvinyl alcohol) 37380-95-3, 9002-89-5; (macrogol) 25322-68-3; (alginic acid) 28961-37-7, 29894-36-8, 9005-32-7, 9005-38-3; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (amylopectin) 9037-22-3; (ethylene vinyl acetate copolymer) 24937-78-8; (polyglactin) 26780-50-7, 34346-01-5; (chitosan) 9012-76-4; (titanium) 7440-32-6

L84 ANSWER 12 OF 26 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:184023 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA13115194281J
TITLE: **Conjugated** suramin or derivatives thereof with **PEG**, polyaspartate or polyglutamate for cancer treatment
AUTHOR(S): Webb, Craig P.; Jeffers, Michael E.; Czerwinski, Gregorz; Michejda, Christopher J.; Vande, Woude George F.
CORPORATE SOURCE: ASSIGNEE: The Government of the United States of America, as Represented by the Secretary, Department of Health and Human Services
PATENT INFORMATION: WO 9943311 A2 2 Sep 1999
SOURCE: (1999) PCT Int. Appl., 44 pp.
CODEN: PIXXD2.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1999:565900
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20030617

ABSTRACT:
The present invention provides an assay that identifies compds. which inhibit cleavage of **HGF**/SF by serum proteases such as uPA, and methods in which such compds. are provided to reaction solns., to cultured cells in vitro, or to a mammal in vivo, to inhibit cleavage of **HGF**/SF (***hepatocyte*** **growth factor**/scatter factor) and to inhibit chemical and biol. effects resulting from the activation of c-Met receptor by **HGF**/SF. The invention also provides methods for modifying suramin and suramin-related polysulfonated compds. that inhibit **HGF**/SF cleavage, by attaching **PEG** or polyanions such as polyglutamate or polyaspartate to the compds. to reduce cellular uptake of the compds., thereby reducing their cytotoxicity. Also provided are a pharmaceutical composition containing at least one polysulfonated **HGF**/SF cleavage-inhibiting compound other than suramin, and a pharmaceutical composition containing at least one **HGF**/SF cleavage-inhibiting form of suramin or a suramin-related polysulfonated compound that is modified by **conjugation** to a chemical moiety that reduces uptake of the compound into cells. The present invention further includes methods wherein such pharmaceutical compns. are administered to a mammal with a tumor that is stimulated to grow by **HGF**/SF, to inhibit the growth or metastasis of the tumor in the mammal.

CLASSIFICATION CODE: 1-6
SUPPLEMENTARY TERMS: Miscellaneous Descriptors
conjugated suramin deriv cancer treatment
REGISTRY NUMBER: 25513-46-6 (Polyglutamic acid)
25608-40-6 (Polyaspartic acid)
26063-13-8 (Polyaspartic acid)
9001-92-7 (Protease)
9039-53-6 (Urokinase-type plasminogen activator)
145-63-1 (Suramin)
314-13-6Q (Evans Blue, polyaspartate and polyglutamate **conjugates**)
241483-26-1 (Suramin **PEG** ester)
72-57-1 (Trypan Blue)
314-13-6 (Evans Blue)
2610-10-8 (Direct Red 80)
2829-43-8 (Direct Red 75)
3214-47-9 (Direct Yellow 50)
3761-53-3 (Xylidine Ponceau 2R)
4196-99-0 (Biebrich Scarlet)

4399-55-7 (Direct Blue 71)
6226-78-4 (Ponceau SS)
6226-79-5 (Ponceau S)
95660-16-5 (C.I. Direct Yellow 62)

REGISTRY NUMBER: 24991-23-9; 6409-90-1; 241483-27-2; 241483-28-3; 241483-29-4; 241483-30-7; 241483-31-8; 241483-32-9; 241483-33-0; 241483-34-1; 241483-35-2; 241483-36-3; 241483-38-5; **25322-68-3**

L84 ANSWER 13 OF 26 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
DUPLICATE 5

ACCESSION NUMBER: 2005-01959 BIOTECHDS

TITLE: Multivalent compound useful for treating disease associated with angiogenesis or hyperproliferation, comprises binding moieties having specificity for different binding sites on same target;
for cancer, arthritis, atherosclerosis, trachoma, corneal graft neovascularization, psoriasis, scleroderma, hemangioma, ocular disease, myocardial angiogenesis, angiofibroma, vulnerary, melanoma, sarcoma and multiple myeloma therapy

AUTHOR: ARBOGAST C; BUSSAT P; FAN H; LINDER K E; MARINELLI E R; NANJAPPAN P; NUNN A; PILLAI R; POCHON S; RAMALINGAM K; SHRIVASTAVA A; SONG B; SWENSON R E; VON WRONSKI M A; SATO A; WALKER S M; DRANSFIELD D T

PATENT ASSIGNEE: ARBOGAST C; BUSSAT P; FAN H; LINDER K E; MARINELLI E R; NANJAPPAN P; NUNN A; PILLAI R; POCHON S; RAMALINGAM K; SHRIVASTAVA A; SONG B; SWENSON R E; VON WRONSKI M A; SATO A; WALKER S M; DRANSFIELD D T

PATENT INFO: US 2004210041 21 Oct 2004

APPLICATION INFO: US 2004-661032 22 Mar 2004

PRIORITY INFO: US 2004-661032 22 Mar 2004; US 2003-440201 15 Jan 2003

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2004-819891 [81]

ABSTRACT: DERWENT ABSTRACT:
NOVELTY - A multivalent compound (I), comprises at least two binding moieties having specificity for different binding sites on the same target.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a diagnostic imaging agent comprising (I) **conjugated** to microbubble or microballon; (2) diagnostic imaging method; (3) method for treating disease by administering a pharmaceutical preparation having (I); (4) treating a disease associated with angiogenesis by administering a pharmaceutical preparation having (I); (5) screening for heteromultimeric compounds having improved binding affinity; and (6) synthesizing (I).

BIOTECHNOLOGY - Preferred Compound: (I) is a multimeric compound comprising several binding moieties. (I) is a dimeric compound. At least one of the binding moieties comprises a polypeptide, preferably all of the binding moieties comprise polypeptides. The affinity of the compound for the target is about 60 or 560 fold greater than the affinity of any one of the polypeptide for the target. Each polypeptide is chosen from Ala-Gly-Trp-Ile-Glu-Cys-Tyr-His-Pro-Asp-Gly-Ile-Cys-Tyr-His-Phe-Gly-Thr, Ala-Gly-Trp-Leu-Glu-Cys-Tyr-Ala-Glu-Phe-Gly-His-Cys-Tyr-Asn-Phe-Gly-Thr, Ala-Gly-Pro-Lys-Trp-Cys-Glu-Glu-Asp-Trp-Tyr-Tyr-Cys-Met-Ile-Thr-Gly-Thr, Gly-Asp-Ser-Arg-Val-Cys-Trp-Glu-Asp-Ser-Trp-Gly-Gly-Glu-Val-Cys-Phe-Arg-Tyr-Asp-Pro, Gly-Asp-Trp-Trp-Glu-Cys-

Lys-Arg-Glu-Glu-Tyr-Arg-Asn-Thr-Thr-Trp-Cys-Ala-Trp-Ala-Asp-Pro, Gly-Asp-Pro-Asp-Thr-Cys-Thr-Met-Trp-Gly-Asp-Ser-Gly-Arg-Trp-Tyr-Cys-Phe-Pro-Ala-Asp-Pro, Ala-Gln-Glu-Pro-Glu-Gly-Tyr-Ala-Tyr-Trp-Glu-Val-Ile-Thr-Leu-Tyr-His-Glu-Glu-Asp-Gly-Asp-Gly-Gly, Ala-Gln-Ala-Phe-Pro-Arg-Phe-Gly-Gly-Asp-Asp-Tyr-Trp-Ile-Gln-Gln-Tyr-Leu-Arg-Tyr-Thr-Asp-Gly-Gly, Ala-Gln-Gly-Asp-Tyr-Val-Tyr-Trp-Glu-Ile-Ile-Glu-Leu-Thr-Gly-Ala-Thr-Asp-His-Thr-Pro-Pro-Gly-Gly, Ala-Gly-Pro-Thr-Trp-Cys-Glu-Asp-Asp-Trp-Tyr-Tyr-Cys-Trp-Leu-Phe-Gly-Thr and Ala-Gln-Asp-Trp-Tyr-Tyr-Asp-Glu-Ile-Leu-Ser-Met-Ala-Asp-Gln-Leu-Arg-His-Ala-Phe-Leu-Ser-Gly-Gly. Optionally, each polypeptide is chosen from Gly-Ser-Phe-Phe-Pro-Cys-Trp-Arg-Ile-Asp-Arg-Phe-Gly-Tyr-Cys-His-Ala-Asn-Ala-Pro-Gly-Gly-Gly-Lys, Ala-Gln-Glu-Trp-Glu-Arg-Glu-Tyr-Phe-Val-Asp-Gly-Phe-Trp-Gly-Ser-Trp-Phe-Gly-Ile-Pro-His-Gly-Gly-Gly-Lys, Gly-Asp-Tyr-Ser-Glu-Cys-Phe-Phe-Glu-Pro-Asp-Ser-Phe-Glu-Val-Lys-Cys-Tyr-Asp-Arg-Asp-Pro-Gly-Gly-Gly-Lys, and Ala-Gly-Pro-Thr-Trp-Cys-Gly-Asp-Asp-Trp-Tyr-Tyr-Cys-Trp-Leu-Phe-Gly-Thr-Gly-Gly-Gly-Lys. The polypeptide comprises an amino acid substitution, and amide bond substitution, D-amino acid substitution, a glycosylated amino acid, a disulfide mimetic substitution, amino acid translocation, retroinverso peptide, peptoid, retroinverso peptoid, or a synthetic peptide. The target is a protein, receptor or a receptor/ligand complex. The binding moieties bind to different epitopes on the protein. The binding moieties bind to different epitopes on the receptor or receptor ligand complex. The target is a receptor involved in angiogenesis. The receptor is a protein tyrosine kinase receptor. The target comprises KDR or KDR/VEGF complex. The binding moieties bind to different epitopes on KDR or KDR/VEGF complex. The target is a receptor involved in hyperproliferation. The target is a receptor expressed on a tumor. The target comprises **hepatocyte growth factor** (**HGF**) receptor (cMet) or **HGF**/cMet complex. The binding moieties bind to different epitopes on cMet or the **HGF**/cMet complex. The binding moieties comprises polypeptides. (I) further comprises at least one labeling group or therapeutic agent. The labeling group or therapeutic agent comprises one or more paramagnetic metal ions or superparamagnetic particles, an ultrasound contrast agent, one or more photolabels, or one or more radionuclides. The paramagnetic metal ion is chosen from Mn(2+), Cu(2+), Fe(2+), Co(2+), Ni(2+), Gd(3+), Eu(3+), Dy(3+), Pr(3+), Cr(3+), Co(3+), Fe(3+), Ti(3+), Tb(3+), Nd(3+), Sm(3+), Ho(3+), Er(3+), Pa(4+) and Eu(2+). (I) comprising labeling group or therapeutic agent further comprises chelator, where the chelator is 1-substituted 1,4,7-tricarboxymethyl 1,4,7,10 tetraazacyclododecane triacetic acid (DO3A) or gadolinium (III). The ultrasound contrast agent comprises a phospholipid stabilized microbubble or a microballon comprising a fluorinated gas. The labeling group or therapeutic agent further comprises a chelator. The chelator comprises DTPA, DOTA, EDTA, TETA, EHPG, HBED, NOTA, DOTMA, TETMA, PDTA, TTHA, LICAM or MECAM. The chelator comprises diethylenetriamine pentaacetic acid, tetraazacyclododecane triacetic acid or their carboxymethyl-substituted derivative. The radionuclide is 18F, 124I, 125I, 131I, 1 123I, 77Br, 76Br, 99mTc, 51Cr, 67Ga, 68Ga, 47Sc, 51Cr, 167Tm, 141Ce, 111In, 168Yb, 175Yb, 140La, 90Y, 88Y, etc. (I) further comprises a compound chosen from seven compounds (e.g., compound (I) and (II)). (I)

comprising a labeling group or therapeutic agent further comprises a linker between the binding moiety and the labeling group or therapeutic agent. The linker comprises substituted or unsubstituted alkyl chain, **polyethylene glycol** derivative, amino acid spacer, sugar, aliphatic spacer, aromatic spacer, lipid molecule or their combinations. The therapeutic agent comprises a bioactive agent, cytotoxic agent, drug, chemotherapeutic agent or radiotherapeutic agent. (I) comprises a dimer chosen from D1, D4, D5, D6, D7, D10, D13, D17, D24, D26, D31, D32 and D33. (I) comprises a dimer having eleven different formulae.

ACTIVITY - Cytostatic; Antiarthritic; antiarteriosclerotic; Antipsoriatic; Dermatological; Ophthalmological; Antiangiogenic; Vulnerary; Antimalarial; Anti-HIV; Antiviral.

MECHANISM OF ACTION - Inhibitor of activity of KDR or cMet; Inhibitor of angiogenesis and/or hyperproliferation; Inhibitor of binding of VEGF to KDR. No supporting data is given.

USE - (I) is useful for treating disease associated with angiogenesis or hyperproliferation such as neoplastic tumor growth (claimed). (I) is useful for delivering detectable label and/or therapeutic agent to the target of interest. (I) is useful in diagnostic imaging and treating various disease state. (I) is useful in gene therapy for treating diseases associated with angiogenesis. (I) is useful for treating cancer, arthritis, atherosclerotic plaques, trachoma, corneal graft neovascularization, psoriasis, scleroderma, hemangioma, ocular diseases, myocardial angiogenesis, angiofibroma, wound granulation, melanoma, sarcoma and multiple myeloma. (I) is useful for treating diseases associated with certain pathogens such as malaria, HIV, SIV, simian hemorrhagic fever virus, etc.

ADMINISTRATION - (I) is administered by parenteral, enteral, or intranasal route in dosages ranging from 0.1 mug/kg-1 mg/kg.

ADVANTAGE - The affinity constant of (I) for its target is greater than the same of constituent polypeptide for the target. (I) improves the activity and/or efficacy of therapeutic agents, e.g., improving their affinity for or residence time at the target. (195 pages)

CLASSIFICATION: THERAPEUTICS, Protein Therapeutics; GENETIC TECHNIQUES and APPLICATIONS, Gene Expression Techniques and Analysis; DISEASE, Cancer; DISEASE, Cardiovascular; DISEASE, Other Diseases

CONTROLLED TERMS: RECOMBINANT PROTEIN PREP., ISOL., VECTOR-MEDIATED GENE TRANSFER, EXPRESSION IN HOST CELL, APPL., CANCER, ARTHRITIS, ATHEROSCLEROSIS, TRACHOMA, CORNEAL GRAFT NEOVASCULARIZATION, PSORIASIS, SCLERODERMA, HEMANGIOMA, OCULAR DISEASE, MYOCARDIAL ANGIOGENESIS, ANGIOFIBROMA, VULNERARY, MELANOMA, SARCOMA, MULTIPLE MYELOMA THERAPY CYTOSTATIC TUMOR ANTIRHEUMATIC (24, 03)

L84 ANSWER 14 OF 26 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-08563 BIOTECHDS
TITLE: Decellularized tissue, useful for producing a medicament for organ implantation, treating subject requiring implantation of tissue or organ or subject at risk of implantation of tissue or organ for prophylaxis;
decellularized tissue production by tissue culture for tissue or organ implantation and transplantation

AUTHOR: SAWA Y; TAKETANI S; IWAI S; MATSUDA H; HARA M; UCHIMURA E; MIYAKE J
PATENT ASSIGNEE: CARDIO INC; NAT INST ADVANCED IND SCI and TECHNOLOGY
PATENT INFO: WO 2004003178 8 Jan 2004
APPLICATION INFO: WO 2003-JP8248 27 Jun 2003
PRIORITY INFO: JP 2002-191527 28 Jun 2002; JP 2002-191527 28 Jun 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-122437 [12]
ABSTRACT: DERWENT ABSTRACT:
NOVELTY - Decellularized tissue (I), where a cell survival rate of the tissue is less than a level at which an immune reaction is elicited in an organism, and the tissue is not damaged to such an extent that hinders the tissue from exhibiting a function which was possessed by the tissue when the tissue was not decellularized, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a tissue graft (II) and a membrane-like tissue graft (III), comprising decellularized tissue, where a cell survival rate of the tissue is less than a level at which an immune reaction is elicited in an organism, the tissue is not damaged to such an extent that hinders the tissue from exhibiting a function which was possessed by the tissue when the tissue was not decellularized, and the tissue has a desired structure; (2) producing (M1) decellularized tissue, comprising providing tissue, and immersing the tissue in a solution containing a non-micellar amphipathic molecule; (3) a decellularized tissue, obtained by (M1); (4) tissue regeneration (M2), comprising: (a) providing decellularized tissue into an organism, where a cell survival rate of the tissue is less than the level at which an immune reaction is elicited in an organism, the tissue is not damaged to such an extent that hinders the tissue from exhibiting a function which was possessed by the tissue when the tissue was not decellularized; and (b) incubating the tissue within the organism for a time sufficient for the tissue to regenerate; (5) producing (M3) a tissue graft, comprising: (a) providing decellularized tissue into an organism, where a cell survival rate of the tissue is less than a level at which an immune reaction is elicited in an organism, the tissue is not damaged to such an extent that hinders the tissue from exhibiting a function which was possessed by the tissue when the tissue was not decellularized; (b) causing a self cell in the organism to infiltrate the decellularized tissue; and (c) incubating the tissue within the organism for a time sufficient for the cell to differentiate; (6) a tissue graft produced by (M3); (7) treating (M4) a subject requiring implantation of tissue or organ or treating a subject at a risk of implantation of tissue or an organ for prophylaxis, comprising: (a) providing decellularized tissue, where a cell survival rate of the tissue is less than a level at which an immune reaction is elicited in an organism, the tissue is not damaged to such an extent that hinders the tissue from exhibiting a function which was possessed by the tissue when the tissue was not decellularized, or a tissue graft comprising the decellularized tissue; and (b) implanting the decellularized tissue or tissue graft to the subject; and (8) a medicament (III) for organ implantation, comprises a decellularized tissue, where a cell survival rate of the tissue is less than a level at which an immune reaction is elicited in an organism, the tissue is not damaged to such an

extent that hinders the tissue from exhibiting a function which was possessed by the tissue when the tissue was not decellularized, or a tissue graft comprising the decellularized tissue.

BIOTECHNOLOGY - Preferred Tissue: In (I), the cell survival rate of the tissue is 30 % or less. The tissue damage rate of the tissue is 30 % or less. The tissue has a tissue strength which permits a clinical application. The tissue has a tissue strength which is 80 % or more of a tissue strength which was possessed by the tissue when the tissue was not decellularized. The tissue has a tissue strength having a beta value which is 80 % or more of a beta value which was possessed by the tissue when the tissue was not decellularized. The tissue has a tissue strength having a beta value of 20 or more. The state of the tissue, in which the tissue is not damaged to such an extent that hinders the tissue from exhibiting a function which was possessed by the tissue when the tissue was not decellularized, includes that an extracellular matrix of the tissue is not substantially degenerated. A survival rate of the extracellular matrix is at least 50 %. Preferred Tissue Graft: In (II), the tissue graft comprises a cell. The cell is a recipient-derived cell. The cell is derived from an organism of the same species as the tissue. The tissue graft comprises no cell. The cell is chosen from vascular endothelial cells, smooth muscle cells, fibroblast, blood cells and precursor cells and somatic stem cells capable of differentiating. Preferred Method: (M1) further involves washing the tissue. The washing step is performed with phosphate buffered saline (PBS). The amphipathic molecule is 1,2-epoxide polymer or **polyethylene glycol** (**PEG**). An average molecular weight of the **PEG** is 200-6000, 1000-2000, or 1500-2000. An average molecular weight of the **PEG** is smaller than or equal to 1000. The immersing step is performed for 30-60 minutes. The immersing step involves physical treatment. The washing step is performed for 3-5 days. The amphipathic molecule is biocompatible. (M1) further involves performing chemical treatment. The chemical treatment is performed with DNase or DNaseI. (M1) further involves disseminating a cell. (M2) further involves providing a cell to the decellularized tissue. The cell is derived from the organism. The cell is present within the organism. The cell is derived from a host homologous or heterologous to the organism. The cell is previously isolated from the organism. The cell is a blood vessel cell or a blood vessel-like cell. (M2) further involves providing a physiologically active substance capable of inducing cell differentiation to the organism. The physiologically active substance is derived from or foreign to the organism. The physiologically active substance is provided in a form of a nucleic acid or a polypeptide. The physiologically active substance is chosen from **hepatocyte growth factor** (**HGF**), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF), platelet derived growth factor (PDGF) and endothelial growth factor (EGF). In (M3), the decellularization tissue comprises a cell. The decellularization tissue is autologous. The decellularization tissue is derived from a homologous or heterologous host. The cell is autologous. (M3) further involves providing a physiologically active substance capable of inducing differentiation of the cell. The physiologically active

substance is a cytokine having hematopoiesis activity. Preferred Medicament: In (III), the tissue is derived from the subject requiring implantation.

USE - (I) is useful for producing a medicament for organ implantation, where a cell survival rate of the tissue is less than the level at which an immune reaction is elicited in an organism, the tissue is not damaged to such an extent that hinders the tissue from exhibiting a function which was possessed by the tissue when the tissue was not decellularized, or a tissue graft comprising the decellularized tissue. The tissue is lumenal tissue. The tissue is tissue chosen from blood vessels, blood vessel-like tissue, cardiac valves, pericardia, durameter, corneas and bones. The tissue is derived from a mammal, preferably, human or swine. (All claimed.) (I) is useful for treating a subject requiring implantation of tissue or an organ, for treating a subject at risk of implantation of tissue or organ for prophylaxis.

ADVANTAGE - (I) has minimum damage to extracellular matrices and can be used on permanent basis.

EXAMPLE - Porcine carotid arteries were prepared from hybrid, and rat aortas were prepared from SD rats under sterile conditions. Freshly collected porcine carotid arteries and rat aortas were placed in phosphate buffered saline (PBS) containing antibiotics to wash out blood components. The blood vessels were then placed in a decellularizing aqueous solution containing **polyethylene glycol** (**PEG**) and allowed to stand for 0.5 hours. The blood vessels were placed in PBS (-) containing antibiotics (100 units of penicillin, 0.1 mg of streptomycin, 0.25 micro-g/ml amphotericin B) on a rotor at room temperature. The wash solution was changed every 24 hours over 72 hours. After rinsing, the blood vessels were immersed in PBS (+) (PBS (-) supplemented with 5 mM MgCl2) containing DNase I at 37 degreesC for 1 hour. The blood vessels were placed in PBS (-) containing antibiotics on a rotor at room temperature. The wash solution was changed every 24 hours over 72 hours. After rinsing, the blood vessels were preserved in PBS (-) containing antibiotics at 4 degreesC. In addition to **PEG** having an average molecular weight of 1000, PEGs having an average molecular weights of 2000, 200 and 6000 were used to perform decellularization treatment. Decellularized tissue was prepared using Triton method or **PEG**/DNaseI method. Paraffin sections (thickness: 3 microm) of a blood vessel graft were prepared and stained with hematoxylin-eosin to identify extracellular matrices. To identify I/IV collagen which was a component of the basal membrane, immunohistochemical staining was used. Aortas of SD rats were fixed with 4 % paraformaldehyde and cryoprotected. Frozen sections (thickness: 5 microm) were prepared, followed by permeabilization with PBS (-) for 3 hours and then blocking with 1% bovine serum albumin in PBS (-) for 1 hour at room temperature. Subsequently, the sections were incubated with primary antibodies and then with secondary antibodies **conjugated** with fluorescein isothiocyanate (FITC). Images were obtained with Zeiss LSM510 confocal microscope. Rat endothelial cell (EC) preparation was performed by killing 5 week old SD rats (180-200 g) with carbon dioxide asphyxiation, followed by removal of their aortas. The aortas were immersed in PBS (-) containing 3 mg/ml of collagenase at 37 degreesC for 30 minutes. The resultant suspension was

centrifuged at 900xg for 4 minutes, and cells were then resuspended in 10 ml Dulbecco's modified Eagle medium (DMEM) plus 10 % fetal calf serum. The cells were prepared at 4x10 to the power 5 cells/ml and incubated in 5 % CO2 at 37 degreesC. A cell survival rate was calculated by counting the number of nuclei in an area of 100 micromx100 microm using a microscope. Specifically, the number of nuclei in the same sample was counted in the area before and after treatment. The number of nuclei in the sample after treatment was divided by the number of nuclei in the sample before treatment and the result was multiplied by 100 to obtain a cell survival rate (%). Results showed a survival rate of 14.6 % and tissue damage rate of 15 % when the tissues were treated with **PEG**/DNaseI treatment and a survival rate of 17.8 % and tissue damage rate of 34 % when the tissues were treated with TRITON treatment. (144 pages)

CLASSIFICATION: THERAPEUTICS, Tissue Culture/Engineering
CONTROLLED TERMS: DECELLULARIZED TISSUE PREP., TISSUE CULTURE, APPL. TISSUE, ORGAN IMPLANTATION, TRANSPLANTATION CELL CULTURE (23, 17)

L84 ANSWER 15 OF 26 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-593275 [57] WPIDS
CROSS REFERENCE: 2004-053022 [05]; 2004-819891 [81]
DOC. NO. NON-CPI: N2004-469230
DOC. NO. CPI: C2004-215754
TITLE: Multivalent compounds with at least two binding moities having specificity for different binding sites on the same target, useful for treating and diagnosing, e.g. angiogenic and hyperproliferative disorders.
DERWENT CLASS: B04 K08 P31 P34 S03
INVENTOR(S): ARBOGAST, C; BUSSAT, P; DRANSFIELD, D T; FAN, H; LINDER, K; MARINELLI, E R; NANJAPPAN, P; NUNN, A; PILLAI, R; POCHON, S; RAMALINGAM, K; SATO, A; SHRIVASTAVA, A; SONG, B; SWENSON, R E; VON WRONSKI, M A; WALKER, S M
PATENT ASSIGNEE(S): (BRAC) BRACCO INT BV; (DYAX-N) DYAX CORP
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004064595	A2	20040805	(200457)*	EN	320	A61B000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SK SL TJ TM TR TT UA UG US UZ VN YU ZW						
AU 2003276884	A1	20040813	(200479)			A61B000-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004064595	A2	WO 2003-US28838	20030911
AU 2003276884	A1	AU 2003-276884	20030911

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003276884	A1 Based on	WO 2004064595

PRIORITY APPLN. INFO: US 2003-379287 20030303; US 2003-440201P 20030115
INT. PATENT CLASSIF.:
MAIN: A61B000-00
BASIC ABSTRACT:
WO2004064595 A UPAB: 20041216
NOVELTY - A multivalent compound (C) comprising at least two binding moieties having specificity for different binding sites on the same target, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a diagnostic imaging agent (A) comprising (C) **conjugated** to a microbubble or microballoon;

(2) a diagnostic imaging method (M1), comprising administering to a patient a pharmaceutical preparation comprising (C), and imaging the compound;

(3) treating (M2) a disease (especially a disease associated with angiogenesis or hyperproliferation) by administering a pharmaceutical preparation comprising (C);

(4) screening (M3) for heteromultimeric compounds having improved binding affinity, comprising:

(a) preparing a labeled compound comprising at least two binding moieties that bind to different binding sites of a target;

(b) contacting the labeled compound with a target;

(c) determining a dissociation constant of the labeled compound; and

(d) comparing the dissociation constant of the labeled compound with the dissociation constant of one or more individual binding moieties;

(5) synthesizing (M4) a multimeric compound comprising at least two binding moieties having specificity for different binding sites on the same target, where at least one of the binding moieties comprises a cyclic polypeptide formed by introducing an amide bond between two side chains, or a polypeptide and a linker comprising at least one glycosylated amino acid chosen from serine, threonine and homoserine; and

(6) synthesizing (M6) a multimeric compound comprising at least two binding moieties having specificity for different binding sites on the same target, chosen from D1, D4, D5, D9, D10, D11, D12, D13, D14, D15, D16, D17, D18, D19, D20, D21, D22, D23, D24, D25, D26 and D27, where the method involves the procedure as disclosed in Example 9 of the specification.

ACTIVITY - Antiarthritic; Cytostatic; Ophthalmological.

MECHANISM OF ACTION - Angiogenesis inhibitor; Kdr tyrosine kinase inhibitor; VEGF antagonist; **Hepatocyte growth factor** antagonist.

The ability of KDR-binding peptides (P2, P3, P6, P7, P8, P9, P10, P11) to inhibit VEGF induced activation of KDR was tested as follows. The peptides were added to human umbilical vein endothelial cells (HUVECs) in the presence of VEGF and were cultured. The KDR phosphorylation was measured by immunoblot assay. The results showed a significant reduction in KDR phosphorylation that indicated the ability of the peptides to inhibit the binding of VEGF to KDR. P2 and P6 were the most potent compounds in the assay to produce 50% inhibition of VEGF-induced KDR phosphorylation at 1 micro m.

USE - (M2) is useful for treating euplastic tumor growth and disease associated with angiogenesis or hyperproliferation (claimed). (C) is useful for treating diseases such as arthritis, atherosclerotic plaques, corneal graft neovascularization or ocular diseases.

ADVANTAGE - (C) is small and can more easily reach a target. (C) localizes more effectively to the target site than other targeting compounds due to its binding to more than one site on the same target.

DESCRIPTION OF DRAWING(S) - The figure shows the specific binding of P5 and P6 to kinase domain region (KDR) in KDR-transfected and mock-transfected cells.

Dwg.1/40

FILE SEGMENT: CPI EPI GMPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B04-B01B; B04-C01; B04-K01J; B05-A03A; B05-A03B; B05-A04; B05-B01P; B05-C07; B11-C07B; B11-C08A; B11-C10; B12-K04E; B14-C09; B14-D06; B14-F02F2; B14-F07; B14-H01; B14-L06; B14-N03; K08-X; K09-B
EPI: S03-E09E

L84 ANSWER 16 OF 26 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-053022 [05] WPIDS
CROSS REFERENCE: 2004-593275 [57]; 2004-819891 [81]
DOC. NO. NON-CPI: N2004-042989
DOC. NO. CPI: C2004-021182
TITLE: New compound with two different binding groups for same target, useful as diagnostic and therapeutic agent, e.g. for tumors and other angiogenic diseases.
DERWENT CLASS: A96 B04 B05 D16 K08 P34
INVENTOR(S): ARBOGAST, C; BUSSAT, P; DRANSFIELD, D T; FAN, H; LINDER, K E; MARINELLI, E R; NANJAPPAN, P; NUNN, A; PILLAI, R; POCHON, S; RAMALINGAM, K; SATO, A; SHRIVASTAVA, A; SONG, B; SWENSON, R E; VON WRONSKI, M A; WALKER, S M; WRONSKI, M A V
PATENT ASSIGNEE(S): (BRAC) BRACCO INT BV; (DYAX-N) DYAX CORP; (ARBO-I) ARBOGAST C; (BUSS-I) BUSSAT P; (DRAN-I) DRANSFIELD D T; (FANH-I) FAN H; (LIND-I) LINDER K E; (MARI-I) MARINELLI E R; (NANJ-I) NANJAPPAN P; (NUNN-I) NUNN A; (PILL-I) PILLAI R; (POCH-I) POCHON S; (RAMA-I) RAMALINGAM K; (SATO-I) SATO A; (SHRI-I) SHRIVASTAVA A; (SONG-I) SONG B; (SWEN-I) SWENSON R E; (WALK-I) WALKER S M; (WRON-I) WRONSKI M A V; (VWRO-I) VON WRONSKI M A
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003084574	A1	20031016	(200405)*	EN	278	A61K051-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
US 2004018974	A1	20040129	(200413)			A61K038-17
AU 2003228276	A1	20031020	(200436)			A61K051-00
EP 1482987	A1	20041208	(200480)	EN		A61K051-00
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR						
US 2005027105	A9	20050203	(200511)			C07K016-44

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003084574	A1	WO 2003-US6656	20030303
US 2004018974	A1 Provisional	US 2002-360821P	20020301
	Provisional	US 2003-440201P	20030115
		US 2003-379287	20030303
AU 2003228276	A1	AU 2003-228276	20030303
EP 1482987	A1	EP 2003-726024	20030303
		WO 2003-US6656	20030303
US 2005027105	A9 Provisional	US 2002-360821P	20020301

Provisional	US 2003-440201P	20030115
CIP of	US 2003-379287	20030303
	US 2003-661032	20030911

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003228276	A1 Based on	WO 2003084574
EP 1482987	A1 Based on	WO 2003084574

PRIORITY APPLN. INFO: US 2003-440201P 20030115; US 2002-360821P 20020301; US 2003-379287 20030303; US 2003-661032 20030911

INT. PATENT CLASSIF.:
MAIN: A61K038-17; A61K051-00; C07K016-44
SECONDARY: A61M036-14; C07K014-47

BASIC ABSTRACT:

WO2003084574 A UPAB: 20050217

NOVELTY - Multivalent compound (I) comprising two binding groups (BG) specific for different binding sites (BS) on the same target, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) diagnostic imaging agent comprising (I) **conjugated** to a microbubble or microballoon;

(2) screening for heteromultimeric compounds having improved binding affinity; and

(3) synthesizing (I).

ACTIVITY - Cytostatic; Antirheumatic; Antiarthritic; Antipsoriatic; Antidiabetic; Ophthalmological; Antiarteriosclerotic; Antiulcer; Vasotropic.

No biological data given.

MECHANISM OF ACTION - Inhibitor of receptor tyrosine kinase activity.

The compound D1, containing peptides (P1) and (P2) connected through a linker, was tested at 10 nM for its effect on phosphorylation of kinase domain region induced by vascular endothelial growth factor in human umbilical vein endothelial cells. It inhibited more than 50 % of phosphorylation at 1 nM, but homodimers (containing two copies of either peptide component) had no effect even at 100 nM.

Ala-Gly-Pro-Thr-Trp-Cys-Glu-Asp-Asp-Trp-Tyr-Tyr-Cys-Trp-Leu-Phe-Gly-Thr-(Gly)3-Lys (P1)

Val-Cys-Trp-Glu-Asp-Ser-Trp-Gly-Gly-Glu-Val-Cys-Phe-Arg-Tyr-Asp-Pro-(Gly)3 (P2)

USE - (I) are used to prepare diagnostic imaging agents and pharmaceutical compositions for treating diseases associated with angiogenesis or hyperproliferation, particularly tumors (claimed) but also rheumatoid arthritis, psoriasis, (diabetic) retinopathy, atherosclerosis, ulcers, restenosis etc., also as contraceptives (by inhibiting uterine neovascularizton). (I) can also be used as analytic reagents for detecting targets in solution.

ADVANTAGE - The use of two different binding groups improves both localization at the target and affinity of binding, with much slower dissociation.

Dwg.0/37

FILE SEGMENT: CPI GMPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: A12-V01; A12-V03C2; B04-K01J; B04-N04; B05-A04; B07-D13; B10-B02; B11-C10; B12-K04B; B12-K04E; B14-C09B; B14-E08; B14-F07; B14-H01; B14-N03; B14-N17C; B14-S04; D05-H09; K08-X; K09-B

L84 ANSWER 17 OF 26 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-790112 [75] WPIDS
CROSS REFERENCE: 2004-178653 [17]
DOC. NO. CPI: C2003-218240
TITLE: Solid phase method, useful for synthesis of new peptide-spacer-lipid **conjugates**, for incorporation into targeted therapeutic liposomes containing therapeutic or diagnostic agents.
DERWENT CLASS: A96 B04
INVENTOR(S): CHANG, T; CHEN, L; SHIH, K; TSENG, C; WU, S; ZENG, J
PATENT ASSIGNEE(S): (BIOT-N) DEV CENT BIOTECHNOLOGY; (BIOT-N) BIOTECHNOLOGY DEV CENT; (CHAN-I) CHANG T; (CHEN-I) CHEN L; (SHIH-I) SHIH K; (TSEN-I) TSENG C; (WUSS-I) WU S
COUNTRY COUNT: 34
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
EP 1319667	A2	20030618	(200375)*	EN	29	C07K001-04
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR						
CA 2413629	A1	20030607	(200375)	EN		C07K007-08
US 2003229013	A1	20031211	(200382)			A61K038-16
CN 1453293	A	20031105	(200408)			C07K017-00
AU 2002313985	A1	20030619	(200460)			C07K017-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1319667	A2	EP 2002-258470	20021209
CA 2413629	A1	CA 2002-2413629	20021205
US 2003229013	A1	US 2001-16569	20011207
CN 1453293	A	CN 2002-155769	20021209
AU 2002313985	A1	AU 2002-313985	20021206

PRIORITY APPLN. INFO: US 2001-16569 20011207
INT. PATENT CLASSIF.:
MAIN: A61K038-16; C07K001-04; C07K007-08; C07K017-00
SECONDARY: A61K009-127; A61K038-31; A61K047-42; A61K047-48; A61P035-00; C07K001-107; C07K007-06; C07K014-00; C07K014-475; C07K014-575; C07K014-775; C07K014-78; C07K017-06; C08G063-48; C08G063-91; G01N033-68

BASIC ABSTRACT:
EP 1319667 A UPAB: 20040920
NOVELTY - A solid phase method for synthesis of new peptide spacer-lipid **conjugates**, and targeted liposomes containing the **conjugates**, is new.
DETAILED DESCRIPTION - A solid phase method for synthesis of new peptide-spacer-lipid **conjugates**, comprises:
(1) synthesizing an amino acid residue protected peptidyl resin in solid phase;
(2) **conjugating** a spacer and a lipid to the peptidyl resin;
(3) cleaving the peptide-spacer-lipid from the peptide-spacer-lipid resin;
(4) removing at least one side chain protecting group from at least one amino acid of the peptide-spacer lipid, forming a peptide-spacer-lipid **conjugate**; and
(5) subjecting the **conjugate** to:
(a) no further processing;
(b) modifying a peptide portion of the **conjugate** to a cyclic form during any of steps (1)-(4) above; or

(c) modifying a peptide portion of the **conjugate** to a cyclic form after any of steps (1)-(4).

The spacer is **conjugated** to each of the peptidyl resin and the lipid by linkage functional groups, the 2 linkage functional groups being the same or different.

INDEPENDENT CLAIMS are also included for:

(1) A peptide-spacer-lipid **conjugate**; and

(2) A targeted therapeutic liposome comprising a peptide-spacer-lipid **conjugate**, and optionally a therapeutic agent for treating a disease or a diagnostic agent for diagnosing a disease.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Somatostain receptor 2 inhibitor.

Binding assay of cyclo-DSPE-NHC(O)-PEG600-C(O)NH-(D)Phe-Cys-Phe-(D)Trp-Lys-Thr-Cys-Thr-ol (c-OPD600) and cyclo-DSPE-NHC(O)-PEG2000-C(O)-NH(D)Phe-Cys-Phe-(D)Trp-Lys-Thr-Cys-Thr-ol (c-OPD2000) **conjugates** with somatostatin receptor 2 (SSTR2) were performed as described in Patel, Y.C and Srikant, C.B, Endocrinology 135, 2814-2817 (1994) and Lipakis, G.et.al.,J.Biol. Chemical 271, 20331-20339 (1996).

The inhibition constants (Ki) for c-OPD600 and c-OPD2000 were 25 nM and 11 nM respectively.

USE - The method is used for the synthesis of peptide-spacer-lipid **conjugates** for incorporation into targeted therapeutic liposomes containing therapeutic or diagnostic agents, e.g. for targeted treatment of a somatostatin receptor expressed cancer (claimed).

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: A12-V01; B04-B01B; B04-C01; B04-C03B; B04-C03C; B04-H01; B04-H06; B04-J10; B04-N06; B05-B01G; B12-M10B; B14-H01; B14-L06

L84 ANSWER 18 OF 26 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-120441 [11] WPIDS
CROSS REFERENCE: 2003-210016 [20]
DOC. NO. CPI: C2003-031027
TITLE: New **conjugate** molecules useful for the selective delivery of therapeutic agents to tumors or other tissues expressing biological receptors.
DERWENT CLASS: A96 B05 B07
INVENTOR(S): KE, S; LI, C; VEGA, J O; WALLACE, S
PATENT ASSIGNEE(S): (KESS-I) KE S; (LICC-I) LI C; (VEGA-I) VEGA J O; (WALL-I) WALLACE S; (TEXA) UNIV TEXAS SYSTEM
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002087497	A2	20021107	(200311)*	EN	46	A61K000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW						
US 2002197261	A1	20021226	(200311)			A61K039-395
AU 2002258895	A1	20021111	(200433)			A61K000-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002087497	A2	WO 2002-US12502	20020419

US 2002197261	A1 Provisional	US 2001-286453P	20010426
	Provisional	US 2001-334969P	20011204
	Provisional	US 2001-343147P	20011220
		US 2002-126369	20020419
AU 2002258895	A1	AU 2002-258895	20020419

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002258895	A1 Based on	WO 2002087497

PRIORITY APPLN. INFO: US 2001-343147P 20011220; US 2001-286453P 20010426; US 2001-334969P 20011204; US 2002-126369 20020419

INT. PATENT CLASSIF.:
MAIN: A61K000-00; A61K039-395
SECONDARY: C07K016-46

BASIC ABSTRACT:

WO 200287497 A UPAB: 20040525

NOVELTY - A new **conjugate** molecule comprising:

(1) a ligand (a);

(2) a polymer spacer (b);

(3) a polymer carrier (c); and

(4) and a therapeutic agent (d)

Where (a) is bonded to (b), (b) is bonded to (c) and (c) is bonded to (d).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) A composition (A1) comprising a nanoparticle, which comprises several **conjugate** molecules;

(2) Selectively delivering (d) to a target tissue in a patient involving administering the **conjugate** molecule to the patient where (a) is with affinity for the target tissue; and

(3) Preparation of the **conjugate** molecule.

ACTIVITY - Cytostatic; Antitumor; Anti-inflammatory; Virucide.

MECHANISM OF ACTION - Tumor growth inhibitor.

USE - For selectively delivering a therapeutic agent to a target tissue (e.g. tumor, (preferably solid tumor selected from breast cancer, ovarian cancer, colon cancer, lung cancer, head and neck cancer, brain cancer, liver cancer, pancreatic cancer, bone cancer, prostate cancer, lymphoma or leukemia), an inflammatory tissue, infectious tissue, a reparative tissue and regenerative tissue) and for treating a patient having a diseased tissue (e.g. the tumor, the inflammatory tissue, infections tissue, the reparative tissue and regenerative tissue) in a patient (e.g. mammal or human) (claimed).

ADVANTAGE - The **conjugate** provide enhanced cellular uptake of the polymeric construct into tumor cells overexpressing EGF receptors and for Her2/neu receptors and maintain the binding affinity of the corresponding monoclonal antibodies. The **conjugate** has improved in vivo half lives and exhibit reduced or eliminated accumulation in the liver. The use of polymers reduces non-specific interaction with non-target tissues and reduces background activity. Attachment of the therapeutic agent and polymer carrier to the ligand with a polymer spacer instead of to the ligand directly improves retention of the ligand's receptor binding affinity. The **conjugate** molecule design strategy is flexible and allows for the preparation of a wide array of molecules for different diagnostic and clinical uses and allows both targeting passive and active targeting.

Dwg.0/13

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: A12-V01; B04-C01; B04-C02C; B04-C02D; B04-C02E; B04-C03B; B04-C03D; B04-G01; B05-A03B; B06-A02; B06-A03; B06-E05; B10-A07; B11-C07A5; B14-A01; B14-C03; B14-H01; B14-S12

L84 ANSWER 19 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2004:145013 USPATFULL
TITLE: Scatter factor/hepatocyte growth factor antagonist NK4 for the treatment of glioma
INVENTOR(S): Brandt, Michael, Iffeldorf, GERMANY, FEDERAL REPUBLIC OF
Brockmann, Marc, Luebeck, GERMANY, FEDERAL REPUBLIC OF
Lamszus, Katrin, Hamburg, GERMANY, FEDERAL REPUBLIC OF
Papadimitriou, Apollon, Bichl, GERMANY, FEDERAL REPUBLIC OF
Schuell, Christine, Penzberg, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004110685	A1	20040610	
APPLICATION INFO.:	US 2003-651807	A1	20030829	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2002-19137	20020830

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HOFFMANN-LA ROCHE INC., PATENT LAW DEPARTMENT, 340 KINGSLAND STREET, NUTLEY, NJ, 07110
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
LINE COUNT: 804
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical composition for the treatment of a tumor derived from glia cells of the central nervous system (CNS) of a patient, characterized in that the composition contains a pharmaceutically acceptable amount of a fragment of the hepatocyte growth factor, the fragment consisting of the N-terminal hairpin domain and the four kringle domains of the hepatocyte growth factor α-chain.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **25322-68-3DP, Polyethylene glycol,**
conjugates with NK4 **313377-05-8DP**, NK4,
conjugates with **polyethylene glycol**
(scatter factor/**hepatocyte growth factor**
fragment NK4 for the treatment of glioma)

L84 ANSWER 20 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2004:40522 USPATFULL
TITLE: Regulation of human skin healing
INVENTOR(S): Herlyn, Meenhard, Wynnewood, PA, UNITED STATES
Berking, Carola, Munich, GERMANY, FEDERAL REPUBLIC OF
Satyamoorthy, Kapaettu, Santhekatte, INDIA
Velazquez, Omaida, Cherry Hill, NJ, UNITED STATES

	NUMBER	KIND	DATE

PATENT INFORMATION: US 2004031067 A1 20040212
APPLICATION INFO.: US 2003-398980 A1 20030822 (10)
WO 2001-US31555 20011011
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HOWSON AND HOWSON, ONE SPRING HOUSE CORPORATION CENTER, BOX 457, 321 NORRISTOWN ROAD, SPRING HOUSE, PA, 19477
NUMBER OF CLAIMS: 57
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 1708
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to new compositions and methods for preparing vascularized dermal reconstructs, vascularized skin grafts, and for enhancing vascularization in situ in response to a variety of medical conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L84 ANSWER 21 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2003:152268 USPATFULL
TITLE: Drugs having long-term retention in target tissue
INVENTOR(S): Sato, Haruya, Kawasaki-shi, JAPAN
Hayashi, Eiko, Kawasaki-shi, JAPAN
Shirae, Hideyuki, Tokyo, JAPAN
PATENT ASSIGNEE(S): AJINOMOTO CO. INC, Tokyo, JAPAN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003103934	A1	20030605
APPLICATION INFO.:	US 2002-259773	A1	20020930 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 2001-JP2604, filed on 28 Mar 2001, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	JP 2000-93775	20000330

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C., 1940 DUKE STREET, ALEXANDRIA, VA, 22314
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 960
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a polyethylene glycol-bound ligand in which polyethylene glycol is bound to a ligand having a binding affinity for a specific receptor or a specific protein (i.e., an antigen), wherein the polyethylene glycol-bound ligand is not internalized into cells, a novel medicament in which a drug is introduced into the polyethylene glycol chain of the ligand, and a pharmaceutical composition containing the same as an effective ingredient

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L84 ANSWER 22 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2003:17026 USPATFULL
TITLE: **PEG conjugates** of NK4
INVENTOR(S): Brandt, Michael, Iffeldorf, GERMANY, FEDERAL REPUBLIC OF
Papadimitriou, Apollon, Bichl, GERMANY, FEDERAL

REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003012775	A1	20030116
APPLICATION INFO.:	US 2002-81309	A1	20020221 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2001-104640	20010223

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HOFFMANN-LA ROCHE INC., PATENT LAW DEPARTMENT, 340 KINGSLAND STREET, NUTLEY, NJ, 07110
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 995
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a conjugate consisting essentially of a NK4 molecule and a polyethylene glycol group having a molecular weight of from about 20 to about 40 kDa. The invention also provides a composition in which the monoPEGylated conjugates comprise at least 90% of the total of pegylated NK4 molecules and unpegylated NK4 molecules in the composition. Also provided is a composition in which the monoPEGylated **conjugates** comprise **conjugates** in which the **PEG** groups are attached to groups randomly selected from the lysine side chains of NK4 molecules and the N-terminal amino groups of NK4 molecules. A method for the treatment of cancer by administering 1 to 30 mg monoPEGylated NK4 per kg per day is further provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **25322-68-3D**, **Polyethylene glycol**, **HGF**
-NK4 **conjugates**
(**PEG-conjugates** of **HGF**-NK4 for antitumor use)

L84 ANSWER 23 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2003:3015 USPATFULL
TITLE: Diagnostic imaging compositions, their methods of synthesis and use
INVENTOR(S): Li, Chun, Missouri City, TX, UNITED STATES
Wen, Xiaoxia, Houston, TX, UNITED STATES
Wu, Qing-Ping, Pearland, TX, UNITED STATES
Wallace, Sidney, Bellaire, TX, UNITED STATES
Ellis, Lee M., Houston, TX, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003003048	A1	20030102
APPLICATION INFO.:	US 2002-126216	A1	20020419 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-286453P	20010426 (60)
	US 2001-334969P	20011204 (60)
	US 2001-343147P	20011220 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Lori D. Stiffler, Baker Botts L.L.P., One Shell Plaza, 910 Louisiana Street, Houston, TX, 77002-4995

NUMBER OF CLAIMS: 105
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 21 Drawing Page(s)
LINE COUNT: 2507
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Conjugate molecules comprising a ligand bonded to a polymer are disclosed. One such conjugate molecule comprises a ligand bonded to a polymer, a chelating agent bonded to the polymer, and a radioisotope chelated to the chelating agent. The conjugate molecules may be useful in detecting and/or treating tumors or biological receptors. These conjugate molecules may be synthesized without the necessity of preactivation of the ligand using an SCN-polymer-chelating agent precursor. Conjugate molecules incorporating an annexin V ligand are particularly useful for visualizing apoptotic cells. Conjugate molecules incorporating a C225 ligand are particularly useful for targeting tumors expressing EGFR.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **25322-68-3DP, PEG,** radiolabeled **conjugates**
(diagnostic imaging compns. comprising radiolabeled **conjugates*****)

L84 ANSWER 24 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2002:343538 **USPATFULL**
TITLE: Therapeutic agent/ligand conjugate compositions, their methods of synthesis and use
INVENTOR(S): Li, Chun, Missouri City, TX, UNITED STATES
Vega, Javier O., Houston, TX, UNITED STATES
Ke, Shi, Missouri City, TX, UNITED STATES
Wallace, Sidney, Bellaire, TX, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002197261	A1	20021226	
APPLICATION INFO.:	US 2002-126369	A1	20020419	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-286453P	20010426	(60)
	US 2001-334969P	20011204	(60)
	US 2001-343147P	20011220	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Lori D. Stiffler, Baker Botts L.L.P., One Shell Plaza, 910 Louisiana Street, Houston, TX, 77002-4995
NUMBER OF CLAIMS: 61
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 1296
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Conjugate molecules comprising a ligand or targeting moiety bonded to a polymer spacer, a polymer carrier bonded to the polymer spacer, and a therapeutic agent bound to the polymer carrier (with or without a linker) are disclosed. The conjugate molecules are useful for the selective delivery of therapeutic agents to tumors or other tissues expressing biological receptors.**

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT *****25322-68-3DP, PEG,** radiolabeled **conjugates**
(diagnostic imaging compns. comprising radiolabeled **conjugates*****)

L84 ANSWER 25 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2001:152765 **USPATFULL**

TITLE: Nucleic acid delivery vehicles
INVENTOR(S): O'Riordan, Catherine R., Boston, MA, United States
Wadsworth, Samuel C., Shrewsbury, MA, United States
PATENT ASSIGNEE(S): Genzyme Corporation, Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6287857	B1	20010911
APPLICATION INFO.:	US 1999-426680		19991025 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. Number WO 1999-US2680, filed on 8 Feb 1999

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-107471P	19981106 (60)
	US 1998-135092P	19981103 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: McKelvey, Terry
ASSISTANT EXAMINER: Sandals, William
LEGAL REPRESENTATIVE: Lazar, Steven R.
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Figure(s); 23 Drawing Page(s)
LINE COUNT: 2871
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes a nucleic acid delivery vehicle construct for transfecting and/or infecting a target cell. The construct is made of a delivery vehicle and a bifunctional complex for linking the delivery vehicle to a target cell. The bifunctional complex has a delivery vehicle-binding molecule or fragment ("delivery vehicle-binding portion"), a molecule or fragment thereof that binds to a cell surface molecule on the target cell ("cell surface molecule-binding portion") and a linker which connects the molecules or fragments.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L84 ANSWER 26 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2000:47214 USPATFULL
TITLE: Methods of enhancing functioning of the upper gastrointestinal tract
INVENTOR(S): Drucker, Daniel J., Ontario, Canada
PATENT ASSIGNEE(S): 1149336 Ontario Inc., Toronto, Canada (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6051557		20000418
APPLICATION INFO.:	US 1998-59504		19980413 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-46754P	19970516 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Tsang, Cecilia J.
ASSISTANT EXAMINER: Delacroix-Muirheid, C.
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 1847
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to glucagon-related peptides and their use for the prevention or treatment of disorders involving the upper gastrointestinal tract including the esophagus and stomach. In particular, it has now been demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause proliferation of the tissue of the upper gastrointestinal tract. Thus, the invention provides methods of proliferating the upper gastrointestinal tract in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the upper gastrointestinal tract, including inflammatory diseases. GLP-2 stimulates the growth of upper gastrointestinal tissue when administered in conjunction with other peptide hormones. The invention further provides pharmaceutical compositions of GLP-2 with at least one other peptide hormone, methods of enhancing the growth of upper gastrointestinal tissue and of gastrointestinal disorders by increasing serum levels of GLP-2 and at least one other peptide hormone, and kits for preforming the methods of the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

FILE 'HOME' ENTERED AT 11:16:54 ON 08 MAR 2005

=>